

46. (Twice amended) A composition for use in synthesizing a nucleic acid molecule comprising one or more enzymes having nucleic acid polymerase activity and one or more isolated amino acids.

Remarks

I. Support for Amendments

Support for the foregoing amendments to the claims may be found throughout the specification. Specifically, the amendments adding the word "isolated" to claims 30 and 46 have been made in response to a suggestion by the Examiner in the present Office Action; support for these amendments can be found *inter alia* from page 26, line 7, through page 28, line 18; more specifically at page 28, lines 12-18. Support for the amendments to claims 35 and 36 may be found in the specification in the paragraph bridging pages 24-25. Accordingly, the present amendments do not add new matter, and their entry is respectfully requested.

II. Status of the Claims

By the foregoing amendments, claims 30, 35, 36, 37, 40, 41, 43, 44 and 46 have been amended. These amendments do not introduce new matter into the application. Upon entry of the foregoing amendments, claims 30-54 are pending in the application, with claims 30 and 46 being the independent claims.

III. Summary of the Office Action

In the Office Action dated November 27, 2000, the Examiner has made seven rejections of the claims. Applicants respectfully offer the following remarks to overcome or traverse each of these elements of the Office Action.

IV. The Rejection of Claims 30-46 Under 35 U.S.C. § 101 is Accommodated

In the Office Action at page 2, sections 3-4, the Examiner has rejected claims 30-46 under 35 U.S.C. § 101, as being directed to non-statutory subject matter. By the foregoing amendments, claims 30 and 46 have been amended, inserting the term "isolated" in accordance with the Examiner's helpful suggestion. Hence, the Examiner's rejection has been fully accommodated. Reconsideration and withdrawal of the rejection are respectfully requested.

V. The Rejection of Claims 30-45 and 50-54, Under 35 U.S.C. § 112, Second Paragraph, is Traversed

In the Office Action at page 3, sections 5-6, the Examiner has rejected claims 30-45 and 50-54 under 35 U.S.C. § 112, second paragraph as being vague and indefinite. Applicants respectfully traverse this portion of the rejection.

A. The Rejection of Claim 30

In making this rejection, the Examiner first contends that:

[c]laim 30 is vague and indefinite because it is unclear why the applicants have not written the formula I to include A and X. It is suggested to rewrite the formula to include A and X to avoid confusion and complication.

Office Action at page 3, section 6, lines 3-6. Applicants respectfully disagree with this contention.

As the Federal Circuit has held, "the primary purpose of the requirement [that one's invention be distinctly claimed] is to guard against unreasonable advantages to the patentee and disadvantages to others arising from uncertainty as to their [respective] rights." *Athletic Alternatives, Inc. v. Prince Manufacturing, Inc.* 73 F.3d 1573, 1581 (Fed. Cir. 1996), citing *General Electric Co. v. Wabash Appliance Corp.*, 304 U.S. 364 (1938). The symbols A and X

of formula I are necessary to properly define the limits of the invention and simplify the description of its scope. If, as the Examiner suggests, the symbols A and X were removed, certain limitations of the claims would either need to be eliminated, or described with more complicated language. For example, claim 31 supplies a proviso to claim 30 that when $q = 1$ and one of $(R_1)_a$, $(R_2)_b$, and $(R_3)_c$ is oxygen and the other two are the same or different and are independently selected from the group consisting of hydrogen, methyl, ethyl and propyl, *then A is not methyl, ethyl, or propyl*. Further, claims 33 and 34 describe embodiments of the invention defined by the identity of the species at the position represented by X.

As such, Applicants respectfully assert that Formula I, as written, particularly points out and distinctly claims the subject matter being claimed. Reconsideration and withdrawal of this portion of the rejection are respectfully requested.

B. The Rejection of Claims 35-39, 41, 43 and 44

The Examiner has also rejected claims 35-39, 41, 43 and 44 as being vague and indefinite. Applicants respectfully traverse this portion of the rejection.

In making this portion of the rejection, the Examiner contends that:

[c]laims 35-39, 41, 43, and 44 are vague and indefinite because it is unclear, of what are the metes and bonds [sic] of the terms "derivatives thereof".

Office Action, page 3, section 6, lines 7-9. Applicants respectfully disagree with this contention.

In the paragraph bridging pages 24-25, the present specification provides a very detailed description of non-limiting examples of derivatives of compounds of formulae I and II that may be used in accordance with the present invention. Moreover, the specification indicates that these derivatives may be synthesized by one of ordinary skill using routine methods of chemical

synthesis. Hence, one of ordinary skill could easily determine the metes and bounds of "derivatives" of the compounds recited in the present claim 1, in view of the teachings of the present specification.

However, to expedite prosecution of the present application, claims 35, 36, 37, 43 and 44 have been amended, removing the phrase "derivatives thereof." As such, this portion of the Examiner's rejection has been fully accommodated. Reconsideration and withdrawal of this portion of the rejection are respectfully requested.

VI. The Rejection of Claims 30-54, Under 35 U.S.C. § 102(a) Over Frackman et al. is Traversed

In the Office Action at page 4, paragraph 8, the Examiner has rejected claims 30-54, under 35 U.S.C. § 102(a), as being anticipated by Frackman *et al. Promega Notes*, 65: 27 (1998). Additionally, this rejection is duplicated in paragraph 11 of the Office Action. Applicants respectfully traverse this rejection.

In making this rejection, the Examiner writes:

Frackman *et al.* [d]iscloses Betaine and DMSO, two PCR enhancing agents. Such agents can be included in PCR amplifications to increase yield, specificity, and consistency.

Office Action, page 4, paragraph 8, lines 4-6. Applicants respectfully offer the following comments in response to the Examiner's rejection.

It is obvious that the structure of DMSO is not encompassed by the claims of the present invention. Likewise, claim 30, as amended, relates to a composition for use in synthesizing a nucleic acid molecule, comprising one or more enzymes having nucleic acid polymerase activity and one or more isolated compounds having a chemical formula selected from the group

consisting of formula I or formula II, or a salt or derivative thereof, wherein said composition is not betaine. Therefore, the present invention, as presented, does not read on betaine. As such, Frackman *et al.* fail to expressly or inherently disclose the composition of claim 30, and therefore cannot and does not anticipate claims 30-54. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(a), and its duplicate in section 11 of the Office Action, are therefore respectfully requested.

VII. The Rejection of Claims 30-54, Under 35 U.S.C. § 102(a) Over Henke et al. is Traversed

In the Office Action at page 4, section 9, the Examiner has rejected claims 30-54 as being anticipated by Henke *et al.* *Nucleic Acid Res.* 25: 3957 (1997). Applicants respectfully traverse this rejection.

In making this rejection, the Examiner contends:

Henke *et al.* [d]isclose Betaine which improves co-amplification.
The inclusion of betaine improves the amplification and is effective with conventional polymerase.

Office Action, page 4, paragraph 9, lines 4-6. Applicants respectfully offer the following comments in response to the Examiner's rejection.

As discussed above, the claims of the current invention, as presented, do not read on betaine. As such, Henke *et al.* fail to expressly or inherently disclose the composition of claim 30, and therefore cannot and does not anticipate claims 30-54. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(a) are therefore respectfully requested.

VIII. The Rejection of Claims 30-54, Under 35 U.S.C. § 102(a) Over Hengen is Traversed

In the Office Action at page 4, section 10, the Examiner has rejected claims 30-54 as being anticipated by Hengen *TIBS* 22: 225 (1997). Applicants respectfully traverse this rejection.

In making this rejection, the Examiner contends:

Hengen discloses the use of betaine in amplification assays. Not only high GC containing targets are more easily amplified but that improvements are also seen in the amount of product.

Office Action, page 4, paragraph 10, lines 3-5. Applicants respectfully offer the following comments in response to the Examiner's rejection.

As discussed above, the claims of the current invention, as presented, do not read on betaine. As such, Hengen fails to expressly or inherently disclose the composition of claim 30, and therefore cannot and does not anticipate claims 30-54. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(a) are therefore respectfully requested.

IX. The Rejection of Claims 30-37 and 42-51, Under 35 U.S.C. § 102(b) Over Joung *et al.* is Traversed

In the Office Action at page 5, section 12, the Examiner has rejected claims 30-37 and 42-51 under 35 U.S.C. § 102(b) as being anticipated by Joung *et al. J. Virol.* 66: 5788 (1992). Applicants respectfully traverse this rejection.

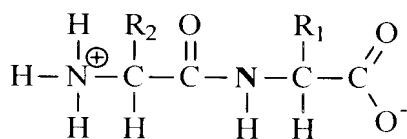
In making this rejection, the Examiner contends:

Joung discloses DNA polymerase assays comprising DNA polymerase activity in the presence of Ad DBP for example. (see page 5790, col. 2).

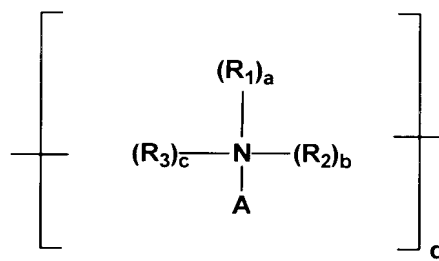
Office Action, page 5, paragraph 12, lines 4-6. Applicants respectfully offer the following comments in response to the Examiner's rejection.

Joung *et al.* disclose methods of DNA elongation and amplification using a polymerase and one of a number of proteins, including adenovirus preterminal protein (pTP), adenovirus DNA-binding protein (ad DBP) and the host factors NFI, NFII and NFIII.

The claims of the present application, as amended, relate to a composition for use in synthesizing a nucleic acid molecule, comprising one or more enzymes having nucleic acid polymerase activity and one or more compounds having a chemical formula selected from the group consisting of formula I and formula II, or a salt or derivative thereof. However, neither formula I nor formula II encompass a naturally occurring protein or polypeptide.



peptide



Portion of Formula I of the presently
claimed invention

In order for formula I of claim 30 to read on a naturally occurring, hetero-polymeric, polypeptide, at least one of R₁, R₂, R₃ or A must be a hydrogen.

The group designated as A cannot be a hydrogen because it is defined as containing a carbon atom bound to the central nitrogen (CR₅); therefore the only other option is for the hydrogen to be represented by R₁, R₂ or R₃.

Claim 1 defines R_1 , R_2 and R_3 as being the same or different, and being independently selected from the group consisting of:

a) $=O$ and;

b) $(W)_g$

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 $-(CR_7)_n$.

Neither selection (a) nor (b) could comprise a hydrogen. If (b) is selected the nitrogen is bound to a carbon which is then bound to R_7 . Therefore, the formula I of claim 30 cannot read on a naturally occurring amino acid.

Finally, assuming that A (which offers the greatest variability among the groups bound to the central nitrogen) represents the amino acid R group, either R_1 , R_2 or R_3 must comprise a carbonyl. In order for this to be true R_7 would have to be a $=O$. However, under claim 30 as currently presented, R_7 is a hydrogen, alkyl, alkenyl, alkynyl, aryl, amino, thiol, mercaptan, halo, nitro, nitrilo, hydroxy, hydroxyalkyl, hydroxyaryl, phosphato, alkoxy, oxide, ether, ester (alkanoyloxy), carboxy, carbonyl, sulfonyl, sulfonic or amido group, none of which are $=O$.

Therefore, applicants respectfully assert that the formulae of claim 30, cannot read on a naturally occurring, hetero-polymeric polypeptide. As such, Juong *et al.* fails to expressly or inherently disclose the composition of claim 30 as currently presented, and therefore cannot and does not anticipate claims 30-37 and 42-51. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) are therefore respectfully requested.

X. Other Matters

Applicants note that the Examiner attached, to the Office Action dated August 9, 2000, initialed copies of the Forms PTO-1449 that were submitted with Applicants' Second and Third Supplemental Information Disclosure Statements filed in the above matter on April 12, 2000, and June 26, 2000, respectively. However, an Examiner-initialed copy of the Form PTO-1449 submitted with Applicants' First Supplemental Information Disclosure statement, filed on April 6, 2000, was not attached, and was not listed on the accompanying Form PTO-326. A copy of the Form PTO-1449 filed on April 6, 2000, and post card receipt date stamped April 6, 2000, is attached herewith. Therefore, Applicants respectfully request that the Examiner provide, with the next communication to Applicants, an initialed copy of this Form PTO-1449 indicating that the document cited thereon has been considered, and also indicate this disposition in the official file wrapper of the present application.

XI. Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this amendment and reply, and allowance of all pending claims, are earnestly solicited.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

A handwritten signature in black ink, appearing to read "Brian J. Del Buono", written over a horizontal line.

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